REMARKS/ARGUMENTS

Claims 1-13 are pending in the instant patent application. The Examiner indicates no claims are allowed. Support for the claim amendments can be found in paragraphs 12, 14, and elsewhere in the application.

Claim Rejections Under 35 U.S.C. § 112

Claims 1-10 and 13 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

The enablement rejection is based on the Examiner's assertion that the claims cover a method of predicting a death of a human being based upon the length of the human's telomere nerve where the death is not associated with any kind of condition such as infectious diseases or physical ailing conditions. The Examiner also asserts that the invention is directed to predicting the survival of an organism where the organism is suffering from some kind of ailment. Based on this characterization, the Examiner asserts that the specification provides neither the guidance nor working examples of this embodiment.

Although applicant does not believe the claims as originally presented are accurately characterized by the Examiner, applicant has amended the claims to all for a method of determining the mortality risk of an organism rather than the survival of an organism. The method comprises determining the telomere length of a somatic cell from the organism and correlating that telomere length with the mortality risk associated with somatic cell telomere length in a population of the organism.

Figures 4 and 5 provide a dramatic demonstration of the subject matter claimed. Figure 4 shows graphs of the survival of a population after age 60. The lines designated "shorter" identify those individuals from the bottom half of the telomere size distribution, whereas the line designated "longer" identifies individuals from the top half of telomere length of distribution.

Figure 5 shows the association of survival as a function of telomere length in subjects aged 60-74 years and in subjects aged 75 years or older. This data clearly shows that there is an association between the telomere length of an individual and that individual's mortality risk.

Further evidence can be found in Table 1 at page 33 of the specification. Table 1 shows the mortality rate ratio as a function of sex and age. It also provides the mortality rate ratio for the specific cause of death. In this regard, mortality rate ratio is the ratio of the death rate for subjects with shorter telomeres to the death rate of subjects with longer telomeres. The mortality rate ratio for "all cause" mortality and heart specific mortality is the ratio of the mortality rate for individuals from the bottom half of the telomere length distribution versus those from the top half of the distribution. In the remaining five categories of cause-specific mortality, the mortality rate ratio is for individuals from the bottom 25% of the telomere length distribution versus the top 75% of the distribution.

This particular analysis was based upon a genomic DNA sampling of 143 research subjects aged 60-97 years who donated blood from 1982 to 1986 to the CEPH collection of cell lines used to build the human genetic linkage map and for whom follow-up survival data were available.

Based upon this disclosure, it can be determined for an individual from this population not only the mortality risk of the individual but also the likelihood of the cause of death.

Based on the foregoing, it is submitted that claims as amended are enabled by the specification.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-3, 8-10 and 13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bechter et al. (*Cancer Research*, 58:4918-4922 (1998)).

Bechter et al. correlates the median telomere length with survival of patients afflicted with B cell chronic lymphocytic leukemia (B-CLL). The median telomere length for these B-CLL patients was 6.0 kb. As shown in Figure 1, those B-CLL patients with a telomere length of less than 6.0 kb had a lower probability of survival as compared to those with a telomere length greater than 6.0 kb.

The claimed invention is distinguishable from Bechter in that Bechter discloses the correlation of the probability of survival as a function of telomere length for a **diseased population**. The claims are not directed to a correlation of an individual's telomere length with the telomere length of a diseased population. As indicated from the working example in the specification, the telomere length is compared the telomere length of a general population. As such, Bechter et al. does not anticipate the claims.

Claims 1-3, 8-10 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chang et al. (*PNAS, USA* 92:11190-11194 (1995)).

Chang et al. analyzed telomere length from tissue samples from the aortic arch, abdominal aorta, iliac artery and iliac vein obtained from autopsies. Figure 3 discloses the mean telomere length as measured by telomere restriction fragments (TRF) for thoracic artery and iliac arteries as a function of donor age. Based on this and the other presented data, the authors conclude that the mean TRF length can serve as a marker for cell turnover of human vascular tissue and that it is possible that telomere length or other measures of cellular senescence could predict the functional status of tissues better than chronological age. See page 11193, column 2, paragraph 3.

The claims are distinguishable over Chang et al. because Chang et al. does not correlate the telomere length of a live individual with the somatic cell telomere length in a general population. Rather, the telomere length of a dead individual is compared with the telomere length of other dead individuals who have died of various causes. In addition, although Chang et al. assert that telomere length is a direct measure of proliferative history, it also acknowledges that to obtain telomere DNA one must obtain a biopsy of endothelial tissue which in itself can induce plaque formation thereby raising ethical and practical difficulties. See Chang 11193, column 2, paragraph 2. Notwithstanding Chang et al.'s assertion of an *in situ* assay for telomere length involving less than 100 cells, there is no disclosure that would facilitate such an assay. Accordingly, Chang et al. would not be applicable to determining the telomere length of endothelial tissue from a live individual.

Claims 1-3 and 6-11 are rejected under 35 § U.S.C. 103(a) as being unpatentable over Palmer et al. (*The Journal of Experimental Medicine* 185(7):1381-1386 (1997)).

According to the Examiner, Palmer et al. disclose a method of correlating the decreased length of telomeres from $CD8^+$ T cells from HIV-infected patients. The Examiner acknowledges that Palmer et al. does not predict the survival of a test patient based on their data. However, the Examiner asserts that Palmer et al. demonstrate the telomere length is decreased in patients infected with HIV and that decreased levels of T cells in humans is correlated with the progression of disease and the survival of patients inflicted with HIV.

However, the claims are patentable over Palmer et al. Palmer et al. uses cells derived from a diseased individual to determine telomere length in $CD8^+$ positive cells. Palmer et al. also compares telomere length with the telomere length of a monozygotic twin rather than a general population. As such, the claims are patentable over Palmer et al.

Claims 4 is rejected under the 35 U.S.C. § 103a as beyond unpatentable over Bechter et al. in view of Kim et al. Bechter is applied as above and Kim is applied for its teaching of an amplification assay of telomerase product.

In addition, Claim 4 is rejected under 35 U.S.C. § 103 as being unpatentable over Chang et al. in view of Kim et al. Chang as applied as above and Kim is applied as above.

Likewise, Claim 4 is rejected under 35 U.S.C. § 103a as being unpatentable over Palmer et al. in view of Kim et al. Palmer is as applied above and Kim is applied as above.

Kim does not cure the deficiencies of Bechter et al., Chang et al and Palmer et al. as applied to Claim 1. Since Claim 1 is patentable over these references, Claim 4 is as well.

Conclusion

Applicants believe the present application is now in condition for allowance. An early and favorable communication thereof is therefore respectfully requested. If the Examiner believes that a telephone conference would expedite prosecution of the application, please call the undersigned at his direct line 415.442.1255.

Respectfully submitted,

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